

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	The Canadian Survey of Health, Lifestyle and Aging with Multiple Sclerosis; Methodology and Initial Results
AUTHORS	Ploughman, Michelle; Beaulieu, Serge; Harris, Chelsea; Hogan, Stephen; Manning, Olivia; Alderdice, Penelope; Fisk, John; Sadvnick, A; O'Connor, Paul; Morrow, Sarah; Metz, Luanne; Smyth, Penelope; Mayo, Nancy; Marrie, Ruth; Knox, Katherine; Stefanelli, Mark; Godwin, Marshall

VERSION 1 - REVIEW

REVIEWER	<p>Prof George A Jelinek Department of Epidemiology and Preventive Medicine, Monash University, Australia</p> <p>Prof Jelinek was diagnosed with MS in 1999. He receives royalties from his books 'Overcoming Multiple Sclerosis: An Evidence-Based Guide to Recovery' and 'Recovering from Multiple Sclerosis: Real-Life Stories of Hope and Inspiration'.</p>
REVIEW RETURNED	02-Jun-2014

GENERAL COMMENTS	<p>Potentially, this is very important research. There is now considerable evidence that MS disease progression is influenced by a variety of modifiable lifestyle risk factors. The long held view that somehow MS is different from other chronic Western degenerative diseases, with a "mind of its own" in terms of disease progression, is no longer tenable. There is an emerging paradigm around secondary and tertiary prevention of this disease, with modification of identified risk factors such as diet, smoking, social isolation, sun exposure, stress and exercise, to positively influence the course of the disease over and above what may be achieved with medication alone.</p> <p>To that end, this is a valuable research methodology, seeking self-reported lifestyle and health behaviours in an aging cohort of people with MS. The authors' assertion that "The uncertainty surrounding MS progression along with aging MS patients warrants the need for investigation into potential disease modifying health behaviours" is strongly supported. While this paper simply reports the methodology in detail, and the characteristics of the cohort, as is appropriate, the authors may have missed an opportunity to more comprehensively assess the lifestyle behaviours of this cohort, given the limitations of the tools used to assess lifestyle behaviours such as diet, discussed below. Given the high uptake of the survey by participants, this would have been an invaluable contribution to the literature. This may yet be possible as an extension to the study, given that the researchers have access to contact information.</p> <p>The Introduction adequately makes the case for this study, making</p>
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	<p>the point that the elderly with MS often are not engaged with MS research and healthcare in general.</p> <p>The Methods are appropriate to the study. In particular, lack of sample size calculation is justified, with recruitment of as large as sample as possible through appropriate targeting of clinics and through media and MS societies. Self-report of diagnosis for those not recruited through neurologists is legitimate, and has previously been used in large scale cross-sectional surveys. (1) It is a little surprising that researchers did not offer the option of an online survey; that may have improved response rate, although it is noted that response rate was high. While many in this group may have been unable to manage online technology, many would, improving response rate and handling of data. Piloting of the questionnaire was a sensible step for this particular patient group. French translation appears to have been handled appropriately for French-speaking participants. Generally, the researchers have used validated questionnaire tools where appropriate. The use of a self-reported co-morbidity questionnaire, previously validated by members of the research team, was appropriate.</p> <p>A major weakness of the study relates to the use of the Simple Lifestyle Indicator Questionnaire. It is important on the one hand to ensure that a questionnaire survey of elderly people is not too onerous and time-consuming, so as to avoid too large a burden on participants, and to ensure adequate response rate. However, this simple one-page survey sheet, while validated in a small study referenced in the paper, collects data that are far too simplistic to make meaningful analysis of risk factor contribution to disease progression possible, and this is where the greatest potential for secondary and tertiary prevention lies. The diet questions for example relate only to salads, fruit and fibre. Data to date indicate that the type and quantity of fat consumed(2, 3) and hence blood lipid profile(4-6) are important determinants of disease progression in people with MS, and this is not able to be assessed at all. While this will be more relevant to future papers where such data are planned to be analysed, it is noted here, and should be discussed in the Limitations.</p> <p>In the Results section, the researchers' methodology and reporting of their treatment of missing data is particularly strong and may serve as a model for other questionnaire-based research.</p> <p>One small point: p13 line 23 reads: 'Participants ranged in age from 55 to 88 years with a mean age of 64.6 years (+/-6.18).' The final figure in brackets should be to one decimal place, so 6.2. Similarly line 30 reads: 'diagnosis by a neurologist was 8.05 years (+/-9.39) with a range' but should read: 'diagnosis by a neurologist was 8.1 years (+/- 9.4) with a range'. Likewise it is probably better to report gender ratio (line 32) to one decimal place ie 3.5:1.</p> <p>The comparison of characteristics of this cohort to the Canadian Community Health Survey is appropriate and enables meaningful comparisons to be made.</p> <p>In Table 3 under Non-Smokers, a total should appear for the researched cohort so that readers may easily see make a comparison with this cohort (91.0%) with the CCHS sample (84.4%).</p> <p>In the Discussion, on p18, line 55, the researchers should reference a large web-based study on smoking and alcohol consumption as it appears to be the biggest sample to date in the area.(7)</p> <p>Overall, it is appropriate to report the methodology of this study, and the characteristics of the sample, in this initial paper. The more important findings are likely to result from further analysis of the associations between the lifestyle variables and outcomes, although this will be limited by the lack of comprehensive data on lifestyle.</p>
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	<p>The discussion and conclusions drawn from this analysis are reasonable.</p> <p>References</p> <ol style="list-style-type: none"> 1. Hadgkiss EJ, Jelinek GA, Weiland TJ, Pereira NG, Marck CH, van der Meer DM. Methodology of an international study of people with multiple sclerosis recruited through web 2.0 platforms: demographics, lifestyle, and disease characteristics. <i>Neurology Research International</i>. 2013;2013:580596. Epub 12/04/2013. 2. Hadgkiss EJ, Jelinek GA, Weiland TJ, Pereira NG, Marck CH, van der Meer DM. The association of diet with quality of life, disability, and relapse rate in an international sample of people with multiple sclerosis. <i>Nutritional neuroscience</i>. 2014. Epub 2014/03/19. 3. Jelinek GA, Hadgkiss EJ, Weiland TJ, Pereira NG, Marck CH, van der Meer DM. Association of fish consumption and Omega 3 supplementation with quality of life, disability and disease activity in an international cohort of people with multiple sclerosis. <i>Int J Neurosci</i>. 2013;123(11):792-800. Epub 2013/05/30. 4. Tettey P, Simpson S, Jr., Taylor B, Blizzard L, Ponsonby AL, Dwyer T, et al. An adverse lipid profile is associated with disability and progression in disability, in people with MS. <i>Mult Scler</i>. 2014. Epub 2014/05/16. 5. Weinstock-Guttman B, Zivadinov R, Horakova D, Havrdova E, Qu J, Shyh G, et al. Lipid profiles are associated with lesion formation over 24 months in interferon-beta treated patients following the first demyelinating event. <i>Journal of neurology, neurosurgery, and psychiatry</i>. 2013;84(11):1186-91. 6. Weinstock-Guttman B, Zivadinov R, Mahfooz N, Carl E, Drake A, Schneider J, et al. Serum lipid profiles are associated with disability and MRI outcomes in multiple sclerosis. <i>Journal of neuroinflammation</i>. 2011;8:127. Epub 2011/10/06. 7. Weiland TJ, Hadgkiss EJ, Jelinek GA, Pereira NG, Marck CH, van der Meer DM. The association of alcohol consumption and smoking with quality of life, disability and disease activity in an international sample of people with multiple sclerosis. <i>J Neurol Sci</i>. 2014;336(1-2):211-9. Epub 2013/12/03.
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REVIEWER	Heleen Beckerman, PhD VU University Medical Center Dept Rehabilitation Medicine The Netherlands
REVIEW RETURNED	02-Jun-2014

GENERAL COMMENTS	<p>1. The objective of the manuscript is not completely clear, and with regard to elaboration somewhat confusing.</p> <p>Quote from the abstract: We aimed 1) to create a profile of aging with MS in Canada focusing on health and lifestyle factors, disability, participation and quality of life in order to 2) determine factors associated with healthy aging.</p> <p>This is confirmed in the introduction: Older individuals who have lived with MS for many years may provide insight into factors that contribute to living a long and healthy life with MS, and in the first sentences of the Discussion section.</p> <p>However, another objective was to recruit 1250 participants..... By partnering with major MS clinic registries and MS society chapters,</p>
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	<p>we hypothesized that we would be able to reach a representative sample of about 5% of the 'aging with MS in Canada' cohort. See also the conclusion on page 19.</p> <p>2. If the latest is the main aim of this paper, then the focus should be on the recruitment and participation of 1250 people with MS. From the flow chart it is noted, however, that only 944 potential participants were contacted. What could be improved in these type future studies?</p> <p>3. Outcomes are clearly defined (e.g. FAI, BI, MSIS-29, mental and cognitive health, social support, see Table 1), but unfortunately most results are not described. So, no complete profile of aging people with MS is given. In the Methods section, there is no consistency in describing the clinimetrics properties of the measurement instruments. Furthermore, it is not clear which instrument was used to describe the mobility problems (details about walking indoor, outdoor, wheelchair, bedridden) of the participants.</p> <p>4. Data entry, page 11. This part could be deleted.</p> <p>5. Canadian Comparison Data. Some further characteristics regarding age distribution, gender, living situation, should be provided to fairly interpret the data given in Table 3. How well did the samples match with each other.</p> <p>6. There is no analysis of determinants of healthy aging with MS.</p> <p>7. Page 18, according to the authors. participants with MS were less physically active. However, Table 3, page 16, shows that 50.3% of the people with MS are moderate to vigorously active, as compared to 26.3% of the Canadian Comparison Cohort.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer 1

1. While this paper simply reports the methodology in detail, and the characteristics of the cohort, as is appropriate, the authors may have missed an opportunity to more comprehensively assess the lifestyle behaviours of this cohort, given the limitations of the tools used to assess lifestyle behaviours such as diet, discussed below. Given the high uptake of the survey by participants, this would have been an invaluable contribution to the literature. This may yet be possible as an extension to the study, given that the researchers have access to contact information.

The reviewer is correct in the assessment of this manuscript. In this paper we focus on the methodology of the survey and the demographics of this cohort. Future

research will examine the impact of lifestyle behaviours on disability, participation and quality of life. The survey was comprehensive but at the expense of some depth in regards to diet behaviours and specific symptom characteristics (i.e. pain, falls).

We do have data regarding use and helpfulness rating of dietary supplements which we intend to report later. As a result of the volume and complexity of the data derived from this study, the results are split into multiple papers that will be submitted following publication of this article.

2. It is a little surprising that researchers did not offer the option of an online survey; that may have improved response rate, although it is noted that response rate was high. While many in this group may have been unable to manage online technology, many would, improving response rate and handling of data.

We did initially plan for an online version. During the pilot testing of this survey it was determined that the majority of people in this cohort preferred a paper version of the survey. This may be because of the age of the group, their disability (vision and coordination) or computer/internet accessibility. We have added in the Methods section "We also determined during this step that participants preferred a paper rather than online version of the survey."

3. A major weakness of the study relates to the use of the Simple Lifestyle Indicator Questionnaire. It is important on the one hand to ensure that a questionnaire survey of elderly people is not too onerous and time-consuming, so as to avoid too large a burden on participants, and to ensure adequate response rate. However, this simple one-page survey sheet, while validated in a small study referenced in the paper, collects data that are far too simplistic to make meaningful analysis of risk factor contribution to disease progression possible, and this is where the greatest potential for secondary and tertiary prevention lies.

We agree with the reviewer's assessment and the use of SLIQ was a major compromise that we felt was necessary because of the length of the survey (36 pages). Because one of the co-authors was a developer of SLIQ, we were aware of further validation that was occurring and has since been published. We have added this limitation to the 'Limitations' section of the paper. "A final limitation of the survey was that we selected the Simple Lifestyle Indicator Questionnaire to assess health behaviours because of its short, simple design, so the data collected lacks detail on diet behaviours which will limit future analysis."

4. One small point: p13 line 23 reads: 'Participants ranged in age from 55 to 88 years with a mean age of 64.6 years (+/-6.18).' The final figure in brackets should be to one decimal place, so 6.2. Similarly line 30 reads: 'diagnosis by a neurologist was 8.05 years (+/-9.39) with a range' but should read: 'diagnosis by a neurologist was 8.1 years (+/- 9.4) with a range'. Likewise it is probably better to report gender ratio (line 32) to one decimal place ie 3.5:1.

We have corrected these errors.

5. In Table 3 under Non-Smokers, a total should appear for the researched cohort so that readers may easily see make a comparison with this cohort (91.0%) with the CCHS sample (84.4%).

This concern has been addressed.

6. In the Discussion, on p18, line 55, the researchers should reference a large web-based study on smoking and alcohol consumption as it appears to be the biggest sample to date in the area.(7)

Thank you. Results of this study are now mentioned in this section and the reference has been added.

Reviewer 2

7. Quote from the abstract: We aimed 1) to create a profile of aging with MS in Canada focusing on health and lifestyle factors, disability, participation and quality of life in order to 2) determine factors associated with healthy aging...However, another objective was to recruit 1250 participants..... By partnering with major MS clinic registries and MS society chapters, we hypothesized that we would be able to reach a representative sample of about 5% of the 'aging with MS in Canada' cohort. See also the conclusion on page 19.

This objective has been added to the abstract. The response rate with respect to the target sample size is mentioned in Results and again in the Conclusion.

8. From the flow chart it is noted that only 944 potential participants were contacted. What could be improved in these type future studies?

Based on feedback from other reviewers (see response to Item 2 above), authors have decided to make mention of an electronic web-based survey that could potentially increase participant numbers. During the pilot study it was determined that the paper copy was most ideal for this cohort however having both options could improve recruitment numbers in the future.

9. Outcomes are clearly defined (e.g. FAI, BI, MSIS-29, mental and cognitive health, social support, see Table 1), but unfortunately most results are not described. So, no complete profile of aging people with MS is given.

The reviewer makes a good point and perhaps because of our intention to complete more analysis for future papers, this paper lacks some detail on the cohort. We have added data that we think provides more information on the cohort derived from the Barthel Index and the Frenchay Activities Index in the form of two new

figures and text in the Results section which is discussed in the Discussion section (all highlighted yellow). Information on mood, co-morbid conditions, social support and resilience are being prepared for future papers. We hope the reviewer finds this addition satisfactory.

10. In the Methods section, there is no consistency in describing the clinometric properties of the measurement instruments. Furthermore, it is not clear which instrument was used to describe the mobility problems (details about walking indoor, outdoor, wheelchair, bedridden) of the participants.

We have now provided the relevant clinometrics for the tools in the Methods section. The information about mobility status is derived from one of the items in the Barthel Index. We have added “ (e.g. mobility from the Barthel Index and lifestyle from the SLIQ)” to the Methods section to explain this.

11. Data entry, page 11. This part could be deleted.

We saved the first sentence of this section and placed it under ‘Data cleaning and imputation’. The remaining is deleted.

12. Canadian Comparison Data. Some further characteristics regarding age distribution, gender, living situation, should be provided to fairly interpret the data given in Table 3. How well did the samples match with each other.

Characteristics including age distribution and gender of the CCHS sample has been added to Table 3. We shifted the age and gender information of our sample from Table 2 to Table 3 as well for comparison. Details of the respondents living situation has been added in the text.

13. There is no analysis of determinants of healthy aging with MS.

We agree that we have provided no analysis of the determinants of healthy aging.

This paper focuses on the methodology and the characteristics of the cohort. We intend to present the influence of health and lifestyle behaviours on disability, participation and health-related quality of life in future publications. We hope that by adding more information on disability and participation as stated above in Q10, the reviewer will find the content satisfactory.

14. Page 18; according to the authors participants with MS were less physically active.

However, Table 3, page 16, shows that 50.3% of the people with MS are moderate to vigorously active, as compared to 26.3% of the Canadian Comparison Cohort.

Table 3 data was correct but in to be sure, we reanalysed the CCHS and our survey data. The questions describing physical activity in the two surveys differ so we matched activity level questions as close as possible. We have added this fact to the limitations section.

We have added the correct data in the Results section Table and text, "Older people with MS were more likely to engage in physical activity (69.4%) compared to typical older Canadians (45.3%)."

We hope the reviewers will be satisfied with the changes we have made to strengthen the manuscript. Again, we are grateful for the constructive feedback.

VERSION 2 – REVIEW

REVIEWER	Professor George A Jelinek Monash University Australia Professor Jelinek was diagnosed with MS in 1999
REVIEW RETURNED	16-Jun-2014

- The reviewer completed the checklist but made no further comments.

REVIEWER	Dr Heleen Beckerman VU University Medical Center Dept Rehabilitation Medicine The Netherlands
REVIEW RETURNED	17-Jun-2014

GENERAL COMMENTS	The authors have satisfactorily incorporated the comments of both reviewers in the revised manuscript.
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